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ORIGINAL RESEARCH ARTICLE

Time-regular pattern analysis on effect of extreme temperature to the death of cerebrovascular and cardiovascular diseases in Chongqing

Yonghong Li[1], Shuquan Luo[2,*], Jinyu He[2], Yibin Cheng[1], Xiaoyuan Yao[1], Bo Sun[1], Yan Wang[1], Yinlong Jin[1,*]

[1] *China Center for Disease Control and Prevention Environmental and Health-Related Product Safety, Beijing 100021, China*

[2] *Chongqing Center for Disease Control and Prevention, Chongqing 400016, China*

*** Corresponding authors:** Shuquan Luo, luosq2006@163.com; Yinlong Jin, jinyinlong1951@ sina.com

ABSTRACT

Objective: to explore the relationship between extreme temperature and death from cardiovascular and cerebrovascular diseases in Chongqing, a "furnace city", and its time regularity. Methods the death data of cardiovascular and cerebrovascular diseases, meteorological and environmental protection data from 2011 to 2013 in Chongqing were collected. The confounding factors such as air pollution, long-term and short-term trends were controlled. The distributed lag nonlinear model (dlnm) was used to analyze the lag effect and cumulative effect of extreme temperature on the death of cardiovascular and cerebrovascular diseases. Results for cerebrovascular disease death, the effect of high temperature was the greatest on the same day (*rr* = 166, 95% CI: 119–233) for 2 days; the influence of low temperature lags 4 days and lasts for 12 days. The maximum *RR* value appears on the 6th day (lag 6) and is 122 (95% CI: 106–141). For ischemic heart disease deaths, the effect of high temperature was greatest on the same day (*rr* = 188, 95% CI: 112–315) for 7 days; the influence of low temperature lags behind for 1 D and lasts for 27 D. The maximum *RR* value appears on the second day (lag 2) and is 205 (95% CI: 132–320). The cumulative risk of extreme high temperature (34 ℃) on death from cerebrovascular disease and ischemic heart disease was 208 (95% CI: 149–290) and 263 (95% CI: 127–542), and the cumulative effects of extreme low temperature (2 ℃) on them were 461 (95% CI: 185–115) and 120 (95% CI: 372–463). Conclusion the lag effect of extreme high temperature and low temperature on the death of the two diseases is different; the cumulative effect of extreme low temperature is higher than that of extreme high temperature, especially on the death of ischemic heart disease.

Keywords: cerebrovascular disease; ischemic heart disease; climate change; extreme temperature; hysteresis effect

1. Introduction

Climate change has led to frequent extreme weather events worldwide[1]. Epidemiological studies have shown that extreme temperatures increase mortality or incidence rate[2]. Cardiovascular disease (especially ischemic heart disease) and cerebrovascular disease have always been the first or important cause of death in many countries, including China[3]. Many studies at home and abroad have analyzed the relationship between extreme temperature and the occurrence or death of cardiovascular and cerebrovascular diseases[4–15]. However, the research results in different regions are not completely consistent. For example, studies in Japan have

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shown that low temperature in winter can increase the death of cardiovascular and cerebrovascular diseases[15] . German research found that extreme high temperature and low temperature can increase the number of emergency patients with cardiovascular diseases[13]. The research results of Astana, the capital of Kazakhstan, showed that there was no correlation between temperature and death from cardiovascular and cerebrovascular diseases[19]. Even in China, the research results of different cities have regional differences[6,20]. Chongqing is one of the "furnace" cities in China. Therefore, it is necessary to analyze the impact of extreme temperature on the mortality of cardiovascular and cerebrovascular diseases in Chongqing and its time regularity, so as to increase more urban research spectrum. Taking Chongqing as the research area, this study aims to analyze the impact of extreme high temperature and low temperature on the death of cardiovascular and cerebrovascular diseases and its time regularity, in order to provide a scientific basis for the effective prevention and control of cardiovascular and cerebrovascular diseases in Chongqing under extreme temperature conditions.

2. Data and methods

2.1. Data sources of death causes of cardiovascular and cerebrovascular diseases

The data used in this study are the cerebrovascular disease and cardiovascular disease death data of Shapingba District, yuzhong District and Qijiang District of Chongqing from 2011 to 2013, provided by the center for Disease Control and prevention in the study area. The death data include the sex, age, permanent address code, prefecture level city, county and district, root cause of death, international classification of diseases (ICD-10) code and date of death. The cause of death data were counted according to the cerebrovascular disease (i60i69) and cardiovascular disease (i20-i25) coded by ICD-10, in which the cardiovascular disease was mainly ischemic heart disease.

2.2. Meteorological and air quality data sources

Meteorological data include daily average, maximum and minimum temperature (℃) and daily average relative humidity (RH, %), which are provided by the local meteorological bureau; air quality data include daily PM_{10} (24 h average concentration, μ G/m^3), so (24 h average concentration, μ G/m^3) and NO_2 (24 h average concentration, μ G/m^3), provided by local environmental protection bureau.

2.3. Statistical analysis

Based on controlling possible confounding factors such as air pollution, relative humidity, long-term trend and day of week effect, the relationship between daily average temperature and cerebrovascular disease and cardiovascular disease death was analyzed by using distributed lag nonlinear model (dlnm). The median daily mean temperature of 17 ℃ during the study period was used as the References temperature. The minimum value of the daily average temperature and the approximate integer value of the 1st and 5th percentile are the extreme low temperatures in this study, which are 2 ℃, 3 ℃ and 5 ℃ respectively; the maximum value of the daily average temperature and the approximate integer values of the 99th and 95th percentiles are extreme high temperatures, which are 34 ℃, 33 ℃ and 31 ℃ respectively. Firstly, the lag effect of extreme temperature on death was analyzed. The lag days were 30 days. The relative risk (*RR*) of different lag days under each extreme temperature was calculated, and then the cumulative effect in the lag period with significant impact under each extreme temperature was calculated.

The basic model formula of dlnm is:

$$E(Y_t) = exp\{\alpha + \beta T_{t,l} + NS(hum, df) + NS(AIR, df) + NS(time, df) + \lambda DOW_t + \varepsilon\}$$

where: $E(Y_t)$—daily death number of cardiovascular (cerebrovascular) disease at *t* days;

α—Intercept, person;

$T_{t,l}$—Variable matrix of daily maximum temperature, ℃;

β— $T_{t,l}$ Coefficient of;

l—lag days, d;

$NS(hum, df)$—The natural cubic spline function of time, the degree of freedom (DF) is 3;

$NS(AIR, df)$—Cubic spline function of air pollutants, degree of freedom (DF) is 3;

$NS(time, df)$—The natural cubic spline function of time, which represents the long-term trend of time, and the degree of freedom (DF) is 7/a;

DOW_t and λ represents the day of the week and its corresponding coefficient, which DOW_t is a dummy variable;

ε—Error term.

The Pearson correlation coefficient between PM_{10}, SO_2 and NO_2 is 0.36–0.46. Therefore, the collinearity of air pollutants in this study is not the main problem[22], and the results after controlling different pollutants are basically the same.

The above statistical analysis was carried out using R software (version 322, rfoundation for Statistical Computing Platform 2015), and the distributed lag nonlinear model was established using dlnm toolkit[22] to analyze the impact of extreme temperature changes on cardiovascular and cerebrovascular diseases.

3. Results

3.1. General situation analysis

The daily death toll, temperature and relative humidity of cerebrovascular disease and cardiovascular disease in the study area from 2011 to 2013 were (667 ± 302), (256 ± 242), 177 ℃ ± 96 ℃ and 737% ± 162% respectively. The daily average concentrations of PM_{10}, sO_2 and NO_2 were 1007 ± 533, 363 ± 172 and (371 ± 133) respectively μg/m^3 (**Table 1**). During the study period, the average annual crude mortality rate in the study area was 620 ‰, and the total deaths of cerebrovascular disease and cardiovascular disease were 7304 and 2803 respectively.

Table 1. General description of deaths from cardiovascular and cerebrovascular diseases, meteorological factors and air pollutants from 2011 to 2013.

Variable	Mean ± SD	Maximum	Median	Minimum value
Daily death of cerebrovascular disease/person	6.67 ± 3.02	22	6	0
Daily death of cardiovascular disease/person	2.56 ± 2.42	15	2	0
Daily average temperature/C	17.7 ± 9.6	34.8	17.6	1.2
Daily average relative humidity/%	73.7 ± 16.2	100	76	26.1
Daily average PMV (|xg/m^3)	100.7 ± 53.3	311	89.7	12.5
Daily average so2/$_{(\|xg/m^3)}$	36.3 ± 17.2	121.8	33.2	4.8
Daily average no2/$_{(\|xg/m^3)}$	37.1 ± 13.3	88.5	36.2	9

3.2. Relationship between Day mean temperature and death from cardiovascular and cerebrovascular diseases

Figure 1 shows the relationship between daily mean temperature and lag time and the risk of cerebrovascular disease and cardiovascular disease death. It can be seen from the figure that both high temperature and low temperature will increase the death risk of cerebrovascular disease and cardiovascular disease, and there is a certain lag effect and persistent effect.

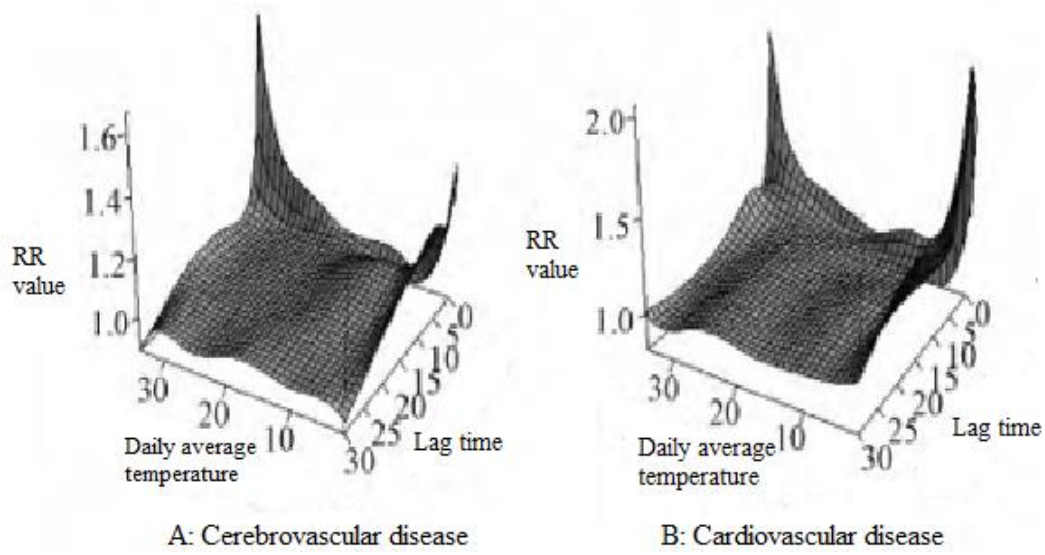

Figure 1. Relationship between daily mean temperature and lag time and risk of cerebrovascular disease and cardiovascular disease death.

3.3. The lag effect of extreme temperature on the death of cardiovascular and cerebrovascular diseases

Figure 2 shows that the effect of high temperature on cerebrovascular disease death is the largest on the day of high temperature, and its effect will last until the second day (lag 1). For example, when the daily average temperature is 34 ℃, 33 ℃ and 31 ℃, the *RR* value of cerebrovascular disease death on the day is the largest, which is 166 (95% CI: 119–233), 147 (95% CI: 112–193) and 126 (95% CI: 101–156). The effect of high temperature on cardiovascular disease death was also the largest on the day of high temperature, and the effect lasted for 7 days. When the daily average temperature was 34 ℃ and 33 ℃, the *RR* value of cardiovascular disease death on the day was the largest, 188 (95% CI: 112–315) and 162 (95% CI: 106–248); when the daily average temperature was 31 ℃, the second day (lag 1) had the greatest impact, and the RR value was 122 (95% CI: 109–137).

The effect of hypothermia on cerebrovascular disease death began to have a significant effect on the 4th day after hypothermia and lasted for about 12 days. The risk of death reached the maximum on the 6th or 7th day. For example, when the daily average temperature was 2 ℃ and 3 ℃, the *RR* value on the 6th day was the maximum, 122 (95% CI: 106–141) and 114 (95% CI: 105–125); when the daily average temperature was 5 ℃, the *RR* value reached the maximum on the 7th day, which was 107 (95% CI: 102–112). The effect of hypothermia on cardiovascular death began to have a significant effect on the first day (lag 1) after hypothermia, and lasted until about the 27th day (lag 27). The risk of death reached the maximum on the second day (lag 2). For example, when the daily average temperature was 2 ℃, 3 ℃ and 5 ℃, the RR value on the second day (lag 2) was 205 (95% CI: 132–320)、161 (95% CI: 119–216) and 121 (95% CI: 101–146).

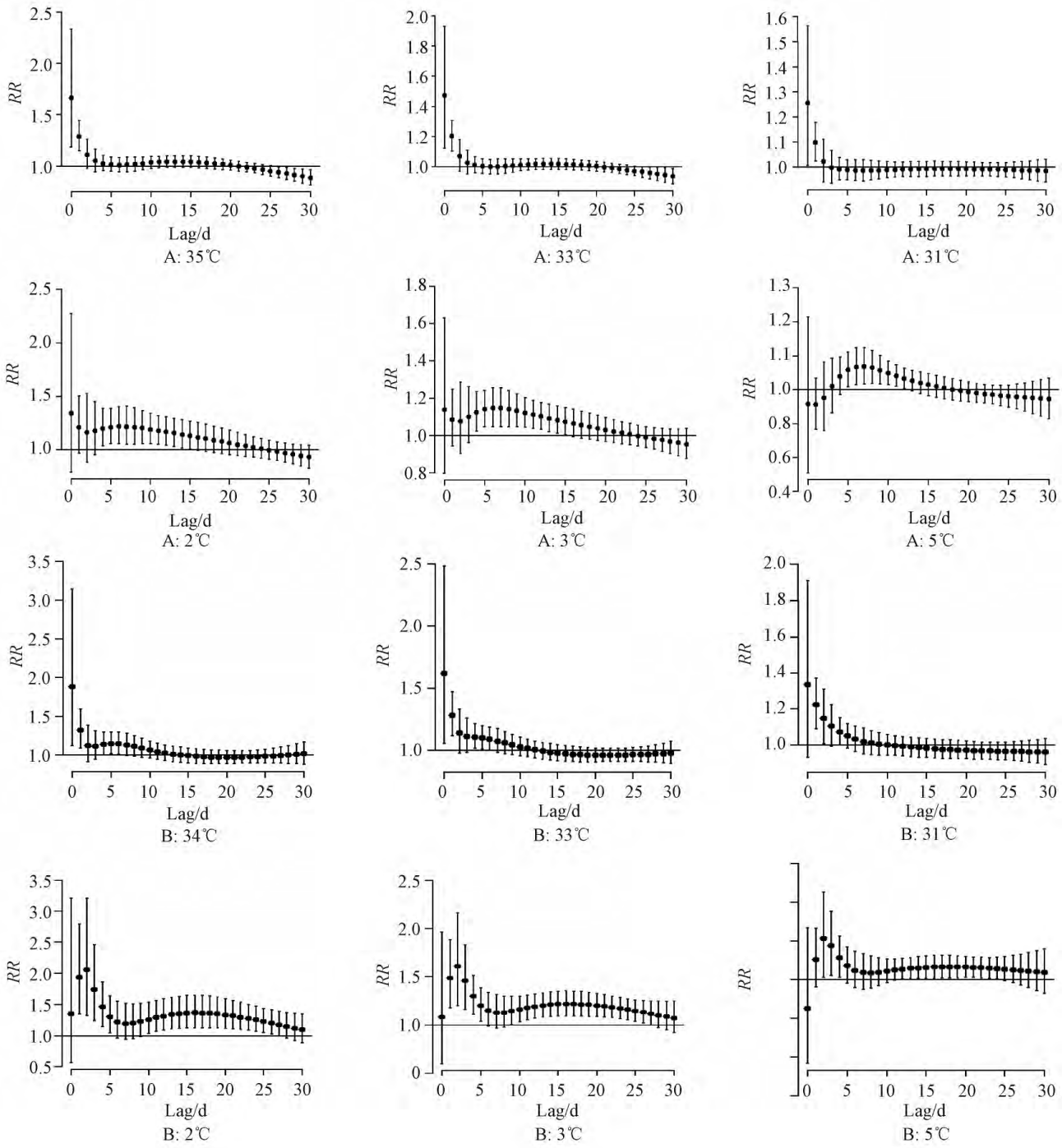

Figure 2. Lag effect of extreme temperature on cerebrovascular disease **(a)** and cardiovascular disease **(b)** death (References temperature: 17 ℃).

3.4. Cumulative effect of extreme temperature on death from cardiovascular and cerebrovascular diseases

According to the lag effect of high temperature and low temperature on cerebrovascular disease and cardiovascular disease death, the cumulative effects of extreme high temperature and low temperature on them are calculated respectively. The results are shown in **Table 2**. The cumulative effect of extreme low temperature is higher than that of extreme high temperature, especially on cardiovascular disease.

Table 2. Cumulative effect of extreme temperature on cerebrovascular disease and cardiovascular disease death.

		RR $_{brain}$ (95%, c1)	**RR $_{heart}$ (95%, cL)**
Extreme high temperature cumulative effect		Lag 0-1	Lag 0-6
	34C	2.08 (1.49, 2.90)	2.63 (1.27, 5.42)
	33C	1.73 (1.33, 2.24)	2.52 (1.54, 4.15)
	31C	1.35 (1.09, 1.67)	2.16 (1.45, 3.21)
Extreme low temperature cumulative effect		Lag 4-45	Lag 1-7
	2C	4.61 (1.85, 11.5)	120.00 (3.72, 463)
	3C	2.88 (1.58, 5.27)	28.30 (3.56, 24)
	5C	1.67 (1.16, 2.40)	5.05 (1.69, 15.1)

Note: Take 17 ℃ as the References temperature.

4. Discussion

This study evaluated the effects of extreme high temperature and low temperature on cardiovascular disease and cerebrovascular disease death in subtropical Chongqing by time series analysis, and further analyzed the cumulative effects of extreme temperature.

This study shows that the impact of extreme high temperature on the death of cardiovascular and cerebrovascular diseases is rapid and short, while the impact of extreme low temperature lags and lasts for a long time. The cumulative effect of extreme low temperature on death is relatively large. Some researchers have found similar results in the studies of Beijing, tianjin, shanghai, wuhan and Guangzhou. The meta-analysis of the results of five cities found that extreme low temperature can increase the death risk of cardiovascular disease by 48%, while extreme high temperature can increase the death risk of cardiovascular disease by 18%[6]. According to the meta-analysis results of Bunker et al.[10], the death rate of cardiovascular disease and cerebrovascular disease increased by 344% (95% CI: 310–378) and 104% (95% CI: 006–275); cardiovascular disease death increased by 166% per 1 ℃ reduction in hypothermia (95% CI: 119–214), the effect of high temperature is more significant. The differences of these research results may be related to the local climate type, the adaptability of residents to the climate and the methods used for data analysis.

In addition, this study also found that in Chongqing, both extreme high temperature and extreme low temperature have a more significant and long-lasting impact on cardiovascular death; moreover, the response time of extreme hypothermia to cardiovascular death was faster. The results are like those of Harbin[20] and Shanghai[23]. The above research results can provide important scientific basis for formulating appropriate early prevention and control measures for different diseases under extreme temperature conditions.

The lag effect has urban difference. The study in Harbin found that high temperature increased the death of cardiovascular and cerebrovascular diseases on the same day and lasted for (0–6) d[20], which is similar to the analysis results of the impact of extreme high temperature on the death of cardiovascular diseases in this study. Guo et al.[6] ound that the extreme cold effect in Beijing, tianjin and Guangzhou lags, while the extreme cold effect in Shanghai and Wuhan occurs earlier. Urban differences should be considered to protect residents' health in response to extreme temperature events, to formulate emergency measures according to local conditions according to the time law of lag effect in different cities.

The effect of extreme temperature on cardiovascular and cerebrovascular diseases is mainly induced by the regulation of related factors in the receptor. Ruan et al.[24] have shown that cold air activities can affect the catecholamine level in human body (such as dopamine, norepinephrine, etc.), which may play an important role in the occurrence of cardiovascular and cerebrovascular diseases. Zheng et al.[12] found a positive

relationship between atmospheric temperature and brain edema volume in patients with acute cerebral hemorrhage. Animal experiments show that high temperature will increase the level of 5-hydroxytryptamine in the body, promote the production of prostaglandins and lead to the increase of local vasodilation and camp, resulting in the increase of blood-brain barrier permeability[2,25]. The destruction of blood-brain barrier promotes the transport of serum protein and water to brain parenchyma[26], which aggravates brain edema and further causes tissue damage or worse.

For example, due to the limited sample size, the study failed to further analyze the impact on the death of different kinds of cardiovascular and cerebrovascular diseases. However, the results of this study can still increase the scientific basis that extreme temperature can increase the death of cardiovascular and cerebrovascular diseases.

Conflict of interest

The authors declare no conflict of interest.

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